

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:44914 CAPLUS
DN 126:139316
TI Oncologic, endocrine & metabolic. Angiogenesis inhibition as a drug target
for disease: an update
AU Seed, Michael P.
CS Dep. Exptl. Pathology, William Harvey Res. Inst., London, EC1M 6BQ, UK
SO Expert Opinion on Investigational Drugs (1996), 5(12), 1617-1637
CODEN: EOIDER; ISSN: 0967-8298
PB Ashley Publications
DT Journal; General Review
LA English
AB A review, with 187 refs. Angiogenesis is required for the development of
many proliferative diseases, including granulomatous disease, such as
rheumatoid arthritis, psoriasis and **neoplasia**, as well as
diabetic retinopathy. A substantial effort is being made to develop
inhibitors of angiogenesis for the treatment of these diseases. This
article is an update of a previous review [Colville-Nash & Seed, Curr.
Opin. Invest. Drugs (1993) 2:763-813], and reviews the recent developments
in the use of: angiostatic steroids, fumagillol derivs., somatostatin
analogs, matrix metalloproteinase (**MMP**) inhibitors, modulators
of vascular endothelial cell growth factor (VEGF), fibroblast growth
factor (FGF), angiostatin, endostatin, platelet factor-4 (PF4),
thrombospondin-1 (TSP-1), cell adhesion mols. (integrins and selectins),
urokinase plasminogen receptor antagonists, cyclo-oxygenase (COX) and
non-steroidal anti-inflammatory drugs (NSAIDs), nitric oxide synthase
(NOS), cytokine-suppressing anti-inflammatory drugs (CSAIDs), and drug
combinations. Most of these approaches have been shown to be
effective in inhibiting tumor growth in vivo, and in many models of
inflammation. The field has, therefore, a very wide range of effective
drug targets which are being exploited. Many areas are still limited by
their reliance on high mol. weight mol. technologies, antibodies and
constructs; however, low mol. weight compds. are now being sought in areas
such as cytokine suppression, VEGF, **MMPs**, COX, NOS, and adhesion
mols. Angiostatic therapy is a rapidly advancing therapeutically viable
and exiting field.
RE.CNT 187 THERE ARE 187 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s mmp and radiation

L31 136 MMP AND RADIATION

=> s antineoplastic agents and radiation

L32 34 ANTINEOPLASTIC AGENTS AND RADIATION

=> s l31 and l32

L33 0 L31 AND L32

=> s l6 and radiation

L34 18 L6 AND RADIATION

=> s l32 and l34

L35 1 L32 AND L34

=> s l31 and l6

Patel

<3/10/2004>

TI Stable inhibition of nuclear factor κ B in **cancer** cells
does not increase sensitivity to cytotoxic drugs
AU Bentires-Alj, Mohamed; Hellin, Anne-Cecile; Ameyur, Maya; Chouaib, Salem;
Merville, Marie-Paule; Bours, Vincent
CS Lab. Med. Chem./Med. Oncol., Univ. Liege, Liege, 4000, Belg.
SO Cancer Research (1999), 59(4), 811-815
CODEN: CNREA8; ISSN: 0008-5472
PB AACR Subscription Office
DT Journal
LA English
AB Several reports indicated that nuclear factor κ B (NF- κ B)
activation by cytokines, cytotoxic drugs, or ionizing **radiation**
protects cells against apoptosis. Therefore, we investigated the
consequence of NF- κ B inhibition on the efficiency of
antineoplastic agents. HPB, HCT116, MCF7, and OVCAR-3
cells stably expressing a dominant neg. I κ B α inhibitor showed
a decreased NF- κ B activation following treatment with tumor necrosis
factor α and various chemotherapeutic agents. However, there was no
difference in survival between parental cells and cells expressing mutated
I κ B α . These studies suggest that, at least in these cell
lines, stable NF- κ B inhibition did not modify the response to
cytotoxic drugs.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:91899 CAPLUS
DN 128:212465
TI Topoisomerase I inhibitors: 1. Topotecan
AU Relias, Valerie; Skirvin, J. Andrew
CS Department of Pharmacy, New England Medical Center, Boston, MA, 02111, USA
SO Journal of Oncology Pharmacy Practice (1997), 3(4), 173-185
CODEN: JOPPFI; ISSN: 1078-1552
PB Appleton & Lange
DT Journal; General Review
LA English
AB A review with 70 refs. on the pharmacol., pharmacokinetics, clin. use, and
adverse effects of the topoisomerase I inhibitor Topotecan. The authors
reviewed the literature through a MEDLINE search of English language
articles from 1985 through 1997. Relevant articles cited in the titles
obtained from the MEDLINE search were also used. The authors reviewed the
current literature in order to discuss the pharmacol., pharmacokinetics,
clin. use, toxicity, drug interactions, indications, formulation, dosage
and administration, and pharmaceutical issues surrounding the use of
Topotecan. The topoisomerase I inhibitors are new **antineoplastic**
agents with a unique mechanism of action. Promising areas of
application include ovarian **cancer**, lung **cancer**,
radiation sensitization, and refractory leukemias. Clin. trials
detailing its activity in these areas are presented.
RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:691872 CAPLUS
DN 125:316004
TI Paclitaxel combination therapy in the treatment of metastatic breast
cancer: A review
AU Holmes, Frankie Ann

- CS M.D. Anderson Cancer Center, University Texas, Houston, TX, 77030, USA
SO Seminars in Oncology (1996), 23(5, Suppl. 11), 46-56
CODEN: SOLGAV; ISSN: 0093-7754
PB Saunders
DT Journal; General Review
LA English
AB A review, with 55 refs. Combinations of active **antineoplastic agents** have been the most effective treatment for metastatic breast **cancer**. Criteria for an effective combination include use of drugs with different mechanisms of action, non-overlapping toxic effects, and synergistic, or at least additive, antitumor activity. Paclitaxel (Taxol), with its unique mechanism of action, offers an excellent opportunity for development of effective combination therapy against breast **cancer**. However, a number of problems have hindered the rapid development of effective combinations. The most obvious problem is the lack of a defined optimal dose and schedule of administration. The second problem has been the demonstration of unexpected interactions between paclitaxel and the other component(s) of the combination, often resulting in unusual and serious toxic effects. This review will focus on the phase I and II trials of paclitaxel in combination with established antineoplastic drugs (except doxorubicin and congeners, which is covered elsewhere in this issue) for breast **cancer**: cisplatin, 5-fluorouracil with or without folinic acid, cyclophosphamide, **radiation** therapy, as well as novel investigational agents or strategies, edatrexate, monoclonal antibodies to oncogenes, growth factors, and gene therapy with insertion of multidrug resistance gene into blood stem cells. Combination therapy offers exciting possibilities of enhanced antitumor efficacy. However, given the unexpected and serious toxic effects observed, only proven combinations should be used outside the context of a clin. trial. Addnl., the burden of proof will be to show that these combinations have increased antitumor activity, decreased toxicity, or both compared with single-agent paclitaxel.
- L28 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:649611 CAPLUS
DN 121:249611
TI Radiotoxicity of platinum-195m-labeled trans-platinum (II) in mammalian cells
AU Howell, Roger W.; Kassiss, Amin I.; Adelstein, S. James; Rao, Dandamudi V.; Wright, Harvel A.; Hamm, Robert N.; Turner, James E.; Sastry, Kandula S. R.
CS University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, NJ, 07103, USA
SO Radiation Research (1994), 140(1), 55-62
CODEN: RAREAE; ISSN: 0033-7587
DT Journal
LA English
AB The chemotoxicity and radiotoxicity of trans-dichlorodiammineplatinum (II) labeled with 195mPt (trans-195mPr) are investigated to ascertain the potential of radioplatinum coordination complexes as **antineoplastic agents**. Platinum-195m, with a half-life of about 4 days, is a prolific emitter of low-energy Auger electrons because of the high probability of internal conversion in its isomeric transitions. The kinetics of cellular uptake and retention after incubation and the radiotoxicity of this Auger electron emitter in the form of trans-195mPt is investigated using cells of the Chinese hamster V79 cell line. The cellular uptake of 195mPt reaches a plateau in about 3 to 5 h of incubation and varies nonlinearly with the extracellular concentration

of radioactivity. The radioactivity is eliminated from the cells after incubation with an effective half-life of 24 h. Cell survival data, when corrected for the chemical toxicity of nonradio-labeled trans-platinum, give a cell survival curve typical for **radiations** with high linear energy transfer. At 37% survival, the mean lethal cellular uptake is about 1.0 mBq/cell. Dosimetric considerations, based on subcellular distribution of the radionuclide, yield a value of 4.8 for the relative biol. effectiveness when compared with 250 kVp x rays. Theor. Monte Carlo track-structure calcns. indicate that the d. of radical species produced in liquid water in the immediate vicinity of a 195mPt decay site is substantially greater than the d. of species along the track of a 5.3 MeV α particle. This explains qual. the efficacy of 195mPt in causing high-LET **radiation** type biol. effects. The extreme radiotoxicity of intranuclearly localized 195mPt, in conjunction with the proclivity of platinum chemotherapy agents to bind to DNA in the cell nucleus, suggests that the combination of chemical effects and the effects of Auger electrons that can be obtained with radioplatinum coordination complexes may have potential in the treatment of **cancer**.

L28 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:112057 CAPLUS
 DN 112:112057
 TI Synergistic antineoplastic pharmaceuticals containing antiemetics and
antineoplastic agents
 IN Pero, Ronald W.
 PA Oxi-Gene, Inc., USA
 SO Eur. Pat. Appl., 11 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN. CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 305008	A2	19890301	EP 1988-201795	19880824
	EP 305008	A3	19900516		
	EP 305008	B1	19940608		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ZA 8805929	A	19890426	US 1987-89477	19870825
				ZA 1988-5929	19880811
				US 1987-89477	19870825
	IL 87525	A1	19940530	IL 1988-87525	19880822
				US 1987-89477	19870825
	AU 8821508	A1	19890302	AU 1988-21508	19880824
	AU 622118	B2	19920402		
				US 1987-89477	19870825
	AT 106749	E	19940615	AT 1988-201795	19880824
				US 1987-89477	19870825
				EP 1988-201795	19880824
	ES 2056902	T3	19941016	ES 1988-201795	19880824
				US 1987-89477	19870825
	CA 1336409	A1	19950725	CA 1988-575624	19880824
				US 1987-89477	19870825
	RU 2080115	C1	19970527	RU 1988-4356575	19880824
				US 1987-89477	19870825
	DK 8804746	A	19890226	DK 1988-4746	19880825
				US 1987-89477	19870825
	JP 01096122	A2	19890414	JP 1988-212320	19880825
	JP 2767590	B2	19980618		

US 5340565

A

19940823

US 1987-89477

19870825

US 1992-896236

19920610

US 1987-89477

19870825

- AB The effectiveness of cytostatic and/or cytotoxic drugs and/or **radiation** in the killing of tumor and/or **cancer** cells is increased by the administration, along with said drugs and **radiation**, of an effective activating or inhibiting amount of a compound or agent which activates or inhibits the chromatin-bound enzyme ADP ribosyltransferase (ADPRT) or the administration of an effective intracellular free Ca^{2+} -increasing amount of a compound which induces cellular or oxidative stress or which acts as an inhibitor or antagonist or calmodulin or Ca^{2+} -calmodulin binding. Suitable such compds. or agents include the phenothiazines, antihistamines, butyrophenones, cannabinoids, corticosteroids, and particularly metoclopramide when employed in combination with cisplatin. Antiemetic metoclopramide (2.0 mg/kg, 3 treatment times), given concomitant to cisplatin (7.5 mg/kg i.p.) and 24 and 48 h after cisplatin administration, potentiated the effect of cisplatin against 2 human squamous cell carcinoma lines xenografted to nude mice. Metoclopramide activated ADPRT and induced cytotoxicity in human mononuclear leukocytes without the addition of other cytostatic agents.

L28 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1981:417893 CAPLUS

DN 95:17893

TI Surgical adjuvant therapy in colon carcinoma: a human tumor spheroid model for evaluating **radiation** sensitizing agents

AU Barone, Robert M.; Calabro-Jones, Paula; Thomas, Thomas N.; Sharp, Thomas R.; Byfield, John E.

CS VA Hosp., La Jolla, CA, USA

SO Cancer (New York, NY, United States) (1981), 47(10), 2349-57

CODEN: CANCAR; ISSN: 0008-543X

DT Journal

LA English

- AB HT-29 human colon tumor cells growing as spheroids were evaluated as a model system for measuring the response of human colon tumor cell to **antineoplastic agents**. HT-29 cells have the capacity to form spheroids up to 1 mm or more in diameter when grown in spinner culture. The multicellular HT-29 spheroids develop hypoxic centers reflecting the cellular conditions found in human **cancer** treatment, i.e., nutritionally deficient hypoxic cells that are felt to be a significant source of both **radiation** and chemotherapy clin. treatment failures. Spheroids of increasing size were radiated and then dispersed into single cells for colony survival assay. Compared with irradiated single cell suspensions, the spheroid cells demonstrated a significant increase in radioresistance. Growing spheroids developed a complex **radiation** survival curve which was variable with respect to size of the spheroid. In direct cytotoxicity assay, 5-fluorouracil (5-FU) exhibited both cytotoxic and cytostatic effects when the drug was present at a concentration $>0.4 \mu\text{g/mL}$. The interaction of 5-FU with x-rays in the HT-29 spheroids was complex and dependent on the type of assay employed (spheroid size vs. clonogenicity). The effect of allopurinol, an agent that protects cells from 5-FU toxicity was also examined. Allopurinol at a concentration of $100 \mu\text{g/mL}$ protected these human colonic carcinoma cells from the cytotoxic effects of 5-FU under conditions resembling those found in vivo. Overall, this HT-29 spheroid system appears to be an interesting model for studying a variety of drug/x-ray interactions in vitro and may prove capable of answering specific questions of preclin. and clin. relevance.

L28 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS ON SIN
AN 1996:691872 CAPLUS
DN 125:316004
TI Paclitaxel combination therapy in the treatment of metastatic breast
cancer: A review
AU Holmes, Frankie Ann

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Page 75

CS M.D. Anderson Cancer Center, University Texas, Houston, TX, 77030, USA
SO Seminars in Oncology (1996), 23(5, Suppl. 11), 46-56
CODEN: SOLGAV; ISSN: 0093-7754
PB Saunders
DT Journal; General Review
LA English
AB A review, with 55 refs. Combinations of active **antineoplastic agents** have been the most effective treatment for metastatic breast **cancer**. Criteria for an effective combination include use of drugs with different mechanisms of action, non-overlapping toxic effects, and synergistic, or at least additive, antitumor activity. Paclitaxel (Taxol), with its unique mechanism of action, offers an excellent opportunity for development of effective combination therapy against breast **cancer**. However, a number of problems have hindered the rapid development of effective combinations. The most obvious problem is the lack of a defined optimal dose and schedule of administration. The second problem has been the demonstration of unexpected interactions between paclitaxel and the other component(s) of the combination, often resulting in unusual and serious toxic effects. This review will focus on the phase I and II trials of paclitaxel in combination with established antineoplastic drugs (except doxorubicin and congeners, which is covered elsewhere in this issue) for breast **cancer**: cisplatin, 5-fluorouracil with or without folinic acid, cyclophosphamide, **radiation** therapy, as well as novel investigational agents or strategies, edatrexate, monoclonal antibodies to oncogenes, growth factors, and gene therapy with insertion of multidrug resistance gene into blood stem cells. Combination therapy offers exciting possibilities of enhanced antitumor efficacy. However, given the unexpected and serious toxic effects observed, only proven combinations should be used outside the context of a clin. trial. Addnl., the burden of proof will be to show that these combinations have increased antitumor activity, decreased toxicity, or both compared with single-agent paclitaxel.

L28 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:91899 CAPLUS

DN 128:212465

TI Topoisomerase I inhibitors: 1. Topotecan

AU Relias, Valerie; Skirvin, J. Andrew

CS Department of Pharmacy, New England Medical Center, Boston, MA, 02111, USA

SO Journal of Oncology Pharmacy Practice (1997), 3(4), 173-185

CODEN: JOPPFI; ISSN: 1078-1552

PB Appleton & Lange

DT Journal; General Review

LA English

AB A review with 70 refs. on the pharmacol., pharmacokinetics, clin. use, and adverse effects of the topoisomerase I inhibitor Topotecan. The authors reviewed the literature through a MEDLINE search of English language articles from 1985 through 1997. Relevant articles cited in the titles obtained from the MEDLINE search were also used. The authors reviewed the current literature in order to discuss the pharmacol., pharmacokinetics, clin. use, toxicity, drug interactions, indications, formulation, dosage and administration, and pharmaceutical issues surrounding the use of Topotecan. The topoisomerase I inhibitors are new **antineoplastic agents** with a unique mechanism of action. Promising areas of application include ovarian **cancer**, lung **cancer**, **radiation** sensitization, and refractory leukemias. Clin. trials detailing its activity in these areas are presented.

RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:691872 CAPLUS

DN 125:316004

TI Paclitaxel combination therapy in the treatment of metastatic breast

cancer: A review

AU Holmes, Frankie Ann

<3/10/2004>

Patel

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:496833 CAPLUS
 DN 127:108945
 TI Preparation of heterocyclic metalloproteinase-inhibitor antitumor agents
 and antiarthritics
 IN Zook, Scott E.; Dagnino, Raymond Jr.; Deason, Michael E.; Bender, Steven
 L.; Melnick, Michael J.
 PA Agouron Pharmaceuticals, Inc., USA; Zook, Scott E.; Dagnino, Raymond Jr.;
 Deason, Michael E.; Bender, Steven L.; Melnick, Michael J.
 SO PCT Int. Appl., 150 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN. CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9720824	A1	19970612	WO 1996-US19328	19961205
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	CA 2238306	AA	19970612	US 1995-569766 A2	19951208
				CA 1996-2238306	19961205
	AU 9714091	A1	19970627	US 1995-569766 A	19951208
	AU 725831	B2	20001019	AU 1997-14091	19961205
				US 1995-569766 A	19951208
	EP 874830	A1	19981104	WO 1996-US19328W	19961205
	EP 874830	B1	20030312	EP 1996-944229	19961205
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
				US 1995-569766 A	19951208
	CN 1207734	A	19990210	WO 1996-US19328W	19961205
				CN 1996-199583	19961205
	BR 9611929	A	19990518	US 1995-569766 A	19951208
				BR 1996-11929	19961205
				US 1995-569766 A	19951208
	NZ 325559	A	20000128	WO 1996-US19328W	19961205
				NZ 1996-325559	19961205
				US 1995-569766 A	19951208
	JP 2000502330	T2	20000229	WO 1996-US19328W	19961205
				JP 1997-521405	19961205
				US 1995-569766 A	19951208

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<3/10/2004>

EP 1095936 A1 20010502
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO

IL 134816 A1 20030212

AT 234291 E 20030315

PT 874830 T 20030630

ES 2195034 T3 20031201

CZ 292942 B6 20040114

ZA 9704954 A 19990105

NO 9802590 A 19980805

US 6153757 A 20001128

US 6500948 B1 20021231

US 2003130506 A1 20030710

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EP 2000-128719 19961205

US 1995-569766 A 19951208

EP 1996-944229 A319961205

IL 1996-134816 19961205

US 1995-569766 A 19951208

IL 1996-124559 A319961205

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AT 1996-944229 19961205

US 1995-569766 A 19951208

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PT 1996-96944229 19961205

US 1995-569766 A 19951208

ES 1996-944229 19961205

US 1995-569766 A 19951208

CZ 1998-1733 19961205

US 1995-569766 A 19951208

ZA 1997-4954 19970605

WO 1996-US19328W 19961205

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US 1995-569766 A 19951208

WO 1996-US19328W 19961205

US 1998-11971 19980629

US 1995-41496P P 19951208

WO 1996-US19328W 19961205

US 1996-759713 A219961206

US 2000-675555 20000929

US 1995-41496P P 19951208

US 1995-569766 B219951208

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US 1996-759713 A219961206

US 1998-11971 A319980629

US 2002-298842 20021118

US 1995-41496P P 19951208

WO 1996-US19328W 19961205

US 1996-759713 W 19961206

US 1998-11971 A319980629

US 2000-675555 A320000929

PATENT FAMILY INFORMATION:

FAN 1998:324822

	PATENT NO.	KIND	DATE
PI	US 5753653	A	19980519
	US 6153757	A	20001128

	US 6500948	B1	20021231
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	US 2003130506	A1	20030710
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APPLICATION NO.	DATE
US 1996-759713	19961206
US 1998-11971	19980629
US 1995-41496P P	19951208
WO 1996-US19328W	19961205
US 1996-759713 A219961206	
US 2000-675555	20000929
US 1995-41496P P	19951208
US 1995-569766 B219951208	
WO 1996-US19328W	19961205
US 1996-759713 A219961206	
US 1998-11971 A319980629	
US 2002-298842	20021118
US 1995-41496P P	19951208
WO 1996-US19328W	19961205

FAN 2000:833554
PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 6153757 A 20001128 US 1998-11971 19980629
US 1995-41496P P 19951208
WO 1996-US19328W 19961205
US 1996-759713 A219961206
WO 1996-US19328 19961205

WO 9720824 A1 19970612
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5753653 A 19980519
US 6500948 B1 20021231

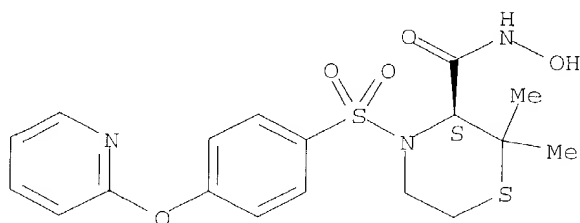
US 2003130506 A1 20030710

US 1995-569766 A219951208
US 1996-759713 19961206
US 2000-675555 20000929
US 1995-41496P P 19951208
US 1995-569766 B219951208
WO 1996-US19328W 19961205
US 1996-759713 A219961206
US 1998-11971 A319980629
US 2002-298842 20021118
US 1995-41496P P 19951208
WO 1996-US19328W 19961205
US 1996-759713 W 19961206
US 1998-11971 A319980629
US 2000-675555 A320000929

OS MARPAT 127:108945
IT 192330-51-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic metalloproteinase-inhibitor antitumor agents and antiarthritics)

RN 192330-51-1 CAPLUS
CN 3-Thiomorpholinecarboxamide, N-hydroxy-2,2-dimethyl-4-[[4-(2-pyridinyloxy)phenyl]sulfonyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Patel

<3/10/2004>

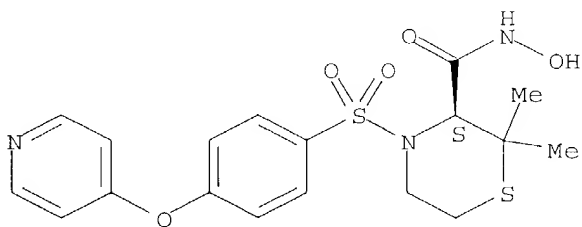
IT 192329-42-3P 192329-58-1P 192330-53-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic metalloproteinase-inhibitor antitumor agents and antiarthritics)

RN 192329-42-3 CAPLUS

CN 3-Thiomorpholinecarboxamide, N-hydroxy-2,2-dimethyl-4-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, (3S)- (9CI) (CA INDEX NAME)

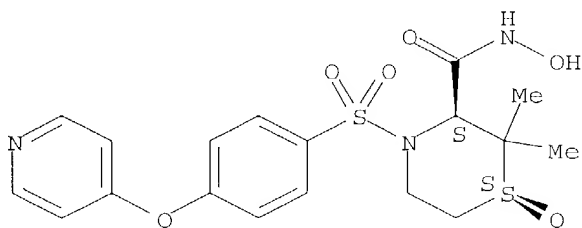
Absolute stereochemistry.



RN 192329-58-1 CAPLUS

CN 3-Thiomorpholinecarboxamide, N-hydroxy-2,2-dimethyl-4-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, 1-oxide, (1S,3S)- (9CI) (CA INDEX NAME)

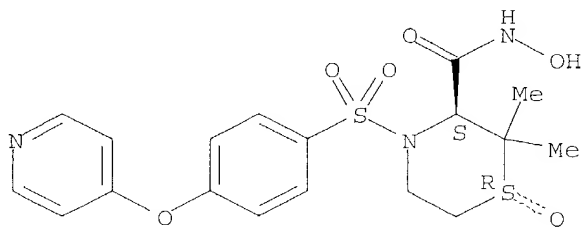
Absolute stereochemistry.



RN 192330-53-3 CAPLUS

CN 3-Thiomorpholinecarboxamide, N-hydroxy-2,2-dimethyl-4-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, 1-oxide, (1R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI For diagram(s), see printed CA Issue.

AB The title compds [I; Z = O, S; V = divalent radical which together with chiral carbon, C*, and N and forms an (un)substituted heterocyclic ring having six ring atoms; A = (un)substituted aryl or heteroaryl], useful as metalloproteinase inhibitors for the treatment of cancer or arthritis, are prepared. Thus, 2(R)-N-hydroxy-1-[4-(4-chlorophenoxy)benzenesulfonyl]-4-(tert-butoxycarbonyl)piperazine-2-carboxamide (m.p. 94.6°), prepared from 2(R)-piperazine-2-carboxylic acid in 4 steps, demonstrated a 77.6% inhibition of lung metastases in a female mouse Lewis lung carcinoma model at 50 mg/kg (i.p.).

Welcome to STN International! Enter x:x

LOGINID:sssptal611sxp

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

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NEWS 19 DEC 22 ABI-INFORM now available on STN
NEWS 20 JAN 27 Source of Registration (SR) information in REGISTRY updated
and searchable
NEWS 21 JAN 27 A new search aid, the Company Name Thesaurus, available in
CA/CAPLUS
NEWS 22 FEB 05 German (DE) application and patent publication number format
changes
NEWS 23 MAR 03 MEDLINE and LMEDLINE reloaded
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NEWS 25 MAR 03 FRANCEPAT now available on STN

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:59:35 ON 10 MAR 2004

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 14:59:45 ON 10 MAR 2004

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STRUCTURE FILE UPDATES: 9 MAR 2004 HIGHEST RN 660815-69-0

DICTIONARY FILE UPDATES: 9 MAR 2004 HIGHEST RN 660815-69-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

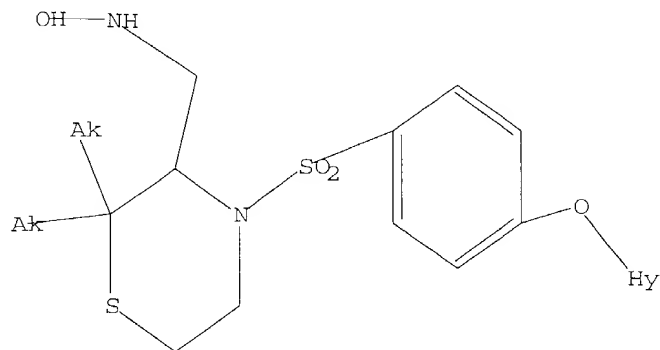
Uploading c:\program files\stnexp\queries\09857995.1

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full

FULL SEARCH INITIATED 15:00:07 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 432 TO ITERATE

100.0% PROCESSED 432 ITERATIONS

12 ANSWERS

SEARCH TIME: 00.00.01

L2 12 SEA SSS FUL L1

=> file marpat

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

155.42

155.63

FILE 'MARPAT' ENTERED AT 15:00:14 ON 10 MAR 2004

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FILE CONTENT: 1988-PRESENT (VOL 140 ISS 10) (20040307/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6683216 27 JAN 2004

DE 10317487 12 FEB 2004

EP 1388563 11 FEB 2004

JP 2004047131 12 FEB 2004

WO 2004011964 05 FEB 2004

Structure search limits have been raised. See HELP SLIMIT for the new, higher limits.

=> s l1 sss full

FULL SEARCH INITIATED 15:00:19 FILE 'MARPAT'

FULL SCREEN SEARCH COMPLETED - 780 TO ITERATE

100.0% PROCESSED 780 ITERATIONS

3 ANSWERS

SEARCH TIME: 00.00.03

Patel

<3/10/2004>

L3 3 SEA SSS FUL L1

=> file caold

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

109.42

265.05

FILE 'CAOLD' ENTERED AT 15:00:33 ON 10 MAR 2004

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FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s ll sss full

REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 15:00:38 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 432 TO ITERATE

100.0% PROCESSED 432 ITERATIONS

12 ANSWERS

SEARCH TIME: 00.00.01

L4 12 SEA SSS FUL L1

L5 0 L4

=> file careact

'CAREACT' IS NOT A VALID FILE NAME

SESSION CONTINUES IN FILE 'CAOLD'

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

Patel

<3/10/2004>

	ENTRY	SESSION
FULL ESTIMATED COST	0.42	421.31

FILE 'CAPLUS' ENTERED AT 15:01:08 ON 10 MAR 2004
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FILE COVERS 1907 - 10 Mar 2004 VOL 140 ISS 11
FILE LAST UPDATED: 9 Mar 2004 (20040309/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L6 3 L3

=> s l4

L7 69 L4

=> d his

(FILE 'HOME' ENTERED AT 14:59:35 ON 10 MAR 2004)

FILE 'REGISTRY' ENTERED AT 14:59:45 ON 10 MAR 2004

L1 STRUCTURE UPLOADED
L2 12 S L1 SSS FULL

FILE 'MARPAT' ENTERED AT 15:00:14 ON 10 MAR 2004

L3 3 S L1 SSS FULL

FILE 'CAOLD' ENTERED AT 15:00:33 ON 10 MAR 2004

S L1

FILE 'REGISTRY' ENTERED AT 15:00:38 ON 10 MAR 2004

L4 12 S L1 SSS FULL

FILE 'CAOLD' ENTERED AT 15:00:39 ON 10 MAR 2004

L5 0 S L4 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:01:08 ON 10 MAR 2004

L6 3 S L3
L7 69 S L4

=> s l2

L8 69 L2

Patel

<3/10/2004>

```
=> s l6 and l7
L9          3 L6 AND L7

=> s mmp and neoplastic agents
L10         0 MMP AND NEOPLASTIC AGENTS

=> s mmp ans neoplasia
L11         0 MMP ANS NEOPLASIA

=> s mmp and cancer
L12        1817 MMP AND CANCER

=> s l12 and neoplasia
L13        21 L12 AND NEOPLASIA

=> s l13 and mmp
L14        21 L13 AND MMP

=> s antineoplastic agents and cancer
L15        498 ANTINEOPLASTIC AGENTS AND CANCER

=> s l15 and neoplasia
L16        4 L15 AND NEOPLASIA

=> ds l9 and l12
DS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l9 and l12
L17        0 L9 AND L12

=> s l9 ans l15
MISSING OPERATOR L9 ANS
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l9 and l15
L18        0 L9 AND L15

=> s l12 and l15
L19        2 L12 AND L15

=> d his

(FILE 'HOME' ENTERED AT 14:59:35 ON 10 MAR 2004)

FILE 'REGISTRY' ENTERED AT 14:59:45 ON 10 MAR 2004
L1          STRUCTURE UPLOADED
L2          12 S L1 SSS FULL

FILE 'MARPAT' ENTERED AT 15:00:14 ON 10 MAR 2004
L3          3 S L1 SSS FULL

FILE 'CAOLD' ENTERED AT 15:00:33 ON 10 MAR 2004
           S L1
```

L4 FILE 'REGISTRY' ENTERED AT 15:00:38 ON 10 MAR 2004
12 S L1 SSS FULL

L5 FILE 'CAOLD' ENTERED AT 15:00:39 ON 10 MAR 2004
0 S L4 SSS FULL

L6 FILE 'CAPLUS' ENTERED AT 15:01:08 ON 10 MAR 2004
3 S L3
L7 69 S L4
L8 69 S L2
L9 3 S L6 AND L7
L10 0 S MMP AND NEOPLASTIC AGENTS
L11 0 S MMP ANS NEOPLASIA
L12 1817 S MMP AND CANCER
L13 21 S L12 AND NEOPLASIA
L14 21 S L13 AND MMP
L15 498 S ANTINEOPLASTIC AGENTS AND CANCER
L16 4 S L15 AND NEOPLASIA
L17 0 S L9 AND L12
L18 0 S L9 AND L15
L19 2 S L12 AND L15

=> d l14 fbib hitstr abs total

L14 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:186011 CAPLUS
TI Analysis of the inflammatory network in benign prostate hyperplasia and prostate **cancer**
AU Koenig, Jens Ekkehard; Senge, Theodor; Allhoff, Ernst Peter; Koenig, Wolfgang
CS Department of Urology, Marienhospital Herne, Ruhr-Universitaet Bochum, Herne, Germany
SO Prostate (New York, NY, United States) (2003), Volume Date 2004, 58(2), 121-129
CODEN: PRSTDS; ISSN: 0270-4137
PB Wiley-Liss, Inc.
DT Journal
LA English
AB INTRODUCTION. The complexity of acute and chronic inflammatory processes may either lead to benign prostate hyperplasia (BPH) and/or prostate **cancer**. Obviously, various tissue cells are activated by chemokines via different chemotaxin receptors which then trigger subsequent processes in angiogenesis, cellular growth, and extravasation as well as **neoplasia**. Using the surgically obtained tissue of patients (n = 36) with BPH or prostate carcinoma (PCA), we studied among others the expression of chemokines (Rantes, IL-8), chemotaxin receptors (CXCR-3 and -4, CCR-3, CCR-5), of matrixmetalloproteinases (MMP -2 and 9), of Toll-like (TL) receptors 1, 2, 3, 4, 5, 7, and 9 and of the inducible cyclooxygenase-2 (cox2) by RT-PCR. Further support for the different properties of tissue from PCA was obtained using two different PCA cell lines (PC3 = androgen resistant cell) or LNCAP cells (androgen sensitive) with emphasis on IL-8, IL-6, and PGE2 release. Cell lines were stimulated with either the tumor necrosis factor- α (TNF- α) and lipopolysaccharide (LPS) over time. In addition to cytokine release, the quantification of mRNA by lightcycler for cox-2, IL-6, and IL-8 was performed on these cell lines. Remarkable differences in expression were obtained by RT-PCR when BPH tissue vs. PCA was analyzed. Expression of

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NEWS 11 DEC 08 IMS file names changed
NEWS 12 DEC 09 Experimental property data collected by CAS now available
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NEWS 14 DEC 17 DGENE: Two new display fields added
NEWS 15 DEC 18 BIOTECHNO no longer updated
NEWS 16 DEC 19 CROPU no longer updated; subscriber discount no longer
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NEWS 17 DEC 22 Additional INPI reactions and pre-1907 documents added to CAS
databases
NEWS 18 DEC 22 IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 19 DEC 22 ABI-INFORM now available on STN
NEWS 20 JAN 27 Source of Registration (SR) information in REGISTRY updated
and searchable
NEWS 21 JAN 27 A new search aid, the Company Name Thesaurus, available in
CA/Caplus
NEWS 22 FEB 05 German (DE) application and patent publication number format
changes
NEWS 23 MAR 03 MEDLINE and LMEDLINE reloaded
NEWS 24 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 25 MAR 03 FRANCEPAT now available on STN

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MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004
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FILE 'HOME' ENTERED AT 15:36:20 ON 10 MAR 2004

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.42

0.42

FILE 'REGISTRY' ENTERED AT 15:37:23 ON 10 MAR 2004

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STRUCTURE FILE UPDATES: 9 MAR 2004 HIGHEST RN 660815-69-0

DICTIONARY FILE UPDATES: 9 MAR 2004 HIGHEST RN 660815-69-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

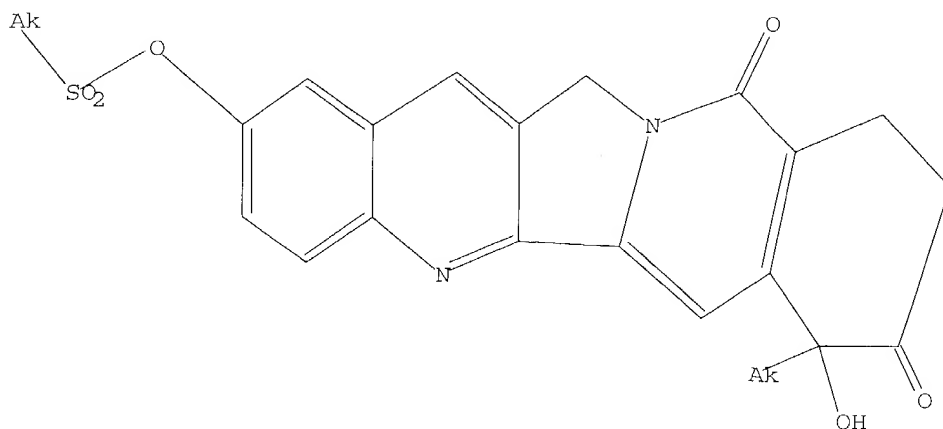
Uploading c:\program files\stnexp\queries\09857995.2

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full

FULL SEARCH INITIATED 15:37:52 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 88 TO ITERATE

100.0% PROCESSED 88 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1

=> file marpat

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

155.42

155.84

FILE 'MARPAT' ENTERED AT 15:38:03 ON 10 MAR 2004

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(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6683216 27 JAN 2004

DE 10317487 12 FEB 2004

EP 1388563 11 FEB 2004

JP 2004047131 12 FEB 2004

WO 2004011964 05 FEB 2004

Structure search limits have been raised. See HELP SLIMIT for the new, higher limits.

=> s l1 sss full

FULL SEARCH INITIATED 15:38:10 FILE 'MARPAT'

FULL SCREEN SEARCH COMPLETED - 206 TO ITERATE

Patel

<3/10/2004>

100.0% PROCESSED 206 ITERATIONS
SEARCH TIME: 00.00.02

0 ANSWERS

L3 0 SEA SSS FUL L1

=> file caold

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

109.42

265.26

FILE 'CAOLD' ENTERED AT 15:38:18 ON 10 MAR 2004
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FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s ll sss full

REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 15:38:28 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 88 TO ITERATE

100.0% PROCESSED 88 ITERATIONS
SEARCH TIME: 00.00.01

0 ANSWERS

L4 0 SEA SSS FUL L1

L5 0 L4

=> file CAREACT

'CAREACT' IS NOT A VALID FILE NAME

SESSION CONTINUES IN FILE 'CAOLD'

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.42	421.52

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 15:38:57 ON 10 MAR 2004
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FILE COVERS 1907 - 10 Mar 2004 VOL 140 ISS 11
FILE LAST UPDATED: 9 Mar 2004 (20040309/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s irinotecan and topotecan

L6 265 IRINOTECAN AND TOPOTECAN

=> s cancer and antineoplastic agents

L7 498 CANCER AND ANTINEOPLASTIC AGENTS

=> s l6 and cancer

L8 150 L6 AND CANCER

=> s cancer and mmps

L9 732 CANCER AND MMPS

=> s l7 and l9

L10 2 L7 AND L9

=> d l10 fbib hitstr abs total

L10 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:441345 CAPLUS

DN 139:115305

TI Matrix metalloproteinases in tumor progression: focus on basal and squamous cell skin **cancer**

AU Kerkela, E.; Saarialho-Kere, U.

CS Department of Dermatology, Helsinki University Central Hospital and Biomedicum Helsinki, University of Helsinki, Finland

SO Experimental Dermatology (2003), 12(2), 109-125

CODEN: EXDEEY; ISSN: 0906-6705

PB Blackwell Munksgaard

DT Journal; General Review

FILE 'CAPLUS' ENTERED AT 15:38:57 ON 10 MAR 2004

L6 265 S IRINOTECAN AND TOPOTECAN
 L7 498 S CANCER AND ANTINEOPLASTIC AGENTS
 L8 150 S L6 AND CANCER
 L9 732 S CANCER AND MMPS
 L10 2 S L7 AND L9
 L11 18 S L6 AND RADIATION
 L12 13 S L11 AND THERAPY
 L13 0 S L6 AND MMPS
 L14 0 S L6 AND L9
 L15 0 S L8 AND L9
 L16 16 S L8 AND RADIATION
 L17 12 S L7 AND RADIATION
 L18 1 S L16 AND L17
 L19 2 S L6 AND L7
 L20 1 S L19 AND RADIATION
 L21 7 S L9 AND RADIATION
 L22 0 S L20 AND L21
 L23 11 S NEOPLASIA AND L6
 L24 4 S NEOPLASIA AND L7
 L25 1 S L23 AND L24
 L26 38 S NEOPLASIA AND MMP
 L27 0 S L26 AND COMBINATION
 L28 2 S L26 AND COMBINATION
 L29 1 S L26 AND RADIATION
 L30 1 S L28 AND L29
 L31 136 S MMP AND RADIATION
 L32 34 S ANTINEOPLASTIC AGENTS AND RADIATION
 L33 0 S L31 AND L32
 L34 18 S L6 AND RADIATION
 L35 1 S L32 AND L34
 L36 0 S L31 AND L6
 L37 108 S L6 AND COMBINATION
 L38 0 S L37 AND RADIATION
 L39 2 S L37 AND MMP
 L40 12 S L32 AND CANCER
 L41 16 S L34 AND CANCER
 L42 0 S L40 AND NEOPLASIA
 L43 0 S L42 AND NEOPLASIA
 L44 1 S L40 AND L41
 L45 12 S L11 AND COMBINATION
 L46 7 S L45 AND L12
 L47 108 S L6 AND COMBINATION
 L48 8 S L47 AND NEOPLASIA
 L49 12 S L47 AND RADIATION
 L50 1 S L48 AND L49
 L51 1 S L48 AND RADIATION

=> d 149 fbib hitstr abs total

L49 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2004:142911 CAPLUS
 TI Attenuated vaccinia viruses and their therapeutic uses against cancer
 IN Kirn, David
 PA USA
 SO PCT Int. Appl., 132 pp.
 CODEN: PIXXD2